Original Article

The Diagnostic Role of Preoperative Blood Tests in Complicated Appendicitis: A Feasible Approach to Surgical Decision

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Abstract

Background: An accurate diagnosis and timely surgical intervention have significant importance in noncomplicated appendicitis (NCA) and complicated appendicitis (CA). Therefore, any factor that helps in the prediction of CA also contributes to suitable treatment options. **Aim:** This retrospective study aimed to identify any relationship between acute appendicitis (AA) and preoperative blood test levels and whether these parameters can differentiate between NCA and CA patients. **Patients and Methods:** A database of 201 appendectomies and 100 control healthy patients was analyzed between 2019 and 2022. Patients were divided into three groups: NCA without peritonitis or phlegmonous appendicitis as group 1; CA with perforated, necrotizing appendicitis with peritonitis as group 2; and the healthy control group (CG) as group 3. White blood cell (WBC), platelet distribution width (PDW), mean platelet volume (MPV), red cell distribution width (RDW), creatine kinase (CK), and bilirubin levels were collected from the patients and compared statistically between the groups. **Results:** Age, WBC, and PDW levels were set as predictive in the differential diagnosis of CA as a result of receiver operating characteristic (ROC) analysis. The multivariate analysis demonstrated that age (OR: 1.023; 95% CI: 1.000–1.045; P = 0.04), male sex (OR: 3.718; 95% CI: 1.501–9.213; P = 0.005), WBC levels (OR: 1.000; 95% CI: 1.000–1.000; P = 0.002), and PDW levels (OR: 2.129; 95% CI: 1.301–3.484; P = 0.003) were independently associated with CA. **Conclusion:** Age, higher WBC count, and PDW levels are valuable in differentiating the diagnosis of CA from NCA, and this could be a feasible approach for surgical decisions.

Keywords: *Acute appendicitis, complicated appendicitis, leukocyte count, platelet distribution width, surgery*

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Introduction

Acute appendicitis (AA) is the most known reason for acute abdominal surgical conditions that accounts for 1–2% of all surgical operations.[1] AA is generally diagnosed with a clinical examination, but clinical signs or complications are not always typical, and a definitive diagnosis can be difficult.[2,3] Although recent evidence has shown that noncomplicated acute appendicitis (NCA) can be treated conservatively without surgery, appendectomy is the appropriate treatment option for complicated acute appendicitis (CA), which includes perforated and gangrenous appendicitis.[4] The inability to fully assess the laboratory tests and unnecessary urgent operation may give rise to the loss of a normal appendix.[5] However, unnecessary delays in surgical treatment may lead to appendix perforation, which is related to morbidity and mortality.[6] CA occurs in 13% to 37% of all cases of appendicitis in adults.[7] An accurate diagnosis and timely surgical intervention have significant importance. Therefore, any factor that

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helps to predict CA also contributes to proper treatment options. Preoperative blood tests are commonly ordered by physicians in the emergency unit for the diagnosis of AA. Increased preoperative blood test levels such as white blood cell (WBC) are the precursor of inflammation in AA. The sensitivity and specificity values vary according to the course of symptoms and defined cutoff values.[7,8] There are some studies that suggest that high bilirubin and C-reactive protein (CRP) levels are the indicators of CA. However, the authors stated that these results have not yet been verified by other studies.[9]

Platelet count (PC) is a commonly used parameter of laboratory blood assessment. Other parameters associated with platelets are mean platelet volume (MPV) and platelet distribution width (PDW).[9,10] Additionally, the red cell distribution width (RDW) may increase the accuracy of AA detection.[9] There is a relationship between thrombocyte activation, thrombosis, and tendency for inflammation.[9,10] As platelet production increases, MPV also increases. The PDW is an indicator of the heterogeneity of thrombocyte volume. Thrombocyte markers, including MPV and PDW, have been related to thrombosis and inflammation. RDW indicates that a variety of erythrocyte sizes and any inflammation may result in increased RDW via incomplete maturation of red blood cells (RBCs) through membrane damage.[9-11] Creatine kinase (CK) levels are significantly elevated following infarction. Ischemic or hemorrhagic intestinal infarcts promote bacterial growth and cause mucosal damage.[12] The breakdown of intestinal smooth muscle cells leads to the release of CK isoenzymes. High CK levels may be particularly useful when evaluated in combination with WBC and bilirubin and physical examination and other laboratory findings in patients with suspected appendicitis symptoms.[12] Although many biochemical markers of AA have been proposed, none of these have been widely adopted. This retrospective study aimed to figure out a relationship between CA and WBC, MPV, PDW, RDW, CK, and bilirubin levels and whether these parameters can differ NCA from CA.

Material and Methods

A database of 232 patients who underwent appendectomy and 100 control patients admitted to the general surgery outpatient clinic was reviewed between January 2019 and October 2021. Twenty-eight noninflamed appendix tissues on final pathology reports were excluded. In total, 204 appendectomy patients and 100 healthy control patients were eligible for the study. All control patients had no chronic disease or inflammation. The study protocol was approved by the hospital ethics committee and performed with the approval of the Ethical Committee of Health Science University Izmir Bozyaka Education and Research Hospital (Approval No. 2021/193).

Initially, a careful history and physical examinations were performed, and the clinical parameters of all patients were recorded. The diagnosis of AA was performed via history, physical examination, radiologic evaluation, and laboratory tests. The Alvarado scoring system was used for all AA patients. Laboratory tests such as WBC, MPV, PDW, RDW, CK, and total bilirubin were studied using a blood count device within one hour after hospital admission. The reference values were 4–10 × 10^9/L for WBCs, 7.5–13.1 femtoliters (fL) for MPV, 10.1–16.1 fL for PDW, 11.6–14.4% for RDW, 0–171 (u/l) for CK, and 0.3–1.2 mg/dl for total bilirubin.

The patients were divided into three groups: NCA without peritonitis or phlegmonous appendicitis as group 1; CA with perforated, plastron, or necrotizing appendicitis with peritonitis as group 2; and the control group (CG) without any inflammation as group 3. WBC, PDW, MPV, RDW, CK count, and bilirubin level were collected from the patients and compared statistically between the groups.

Statistical analysis

All data were entered into the Statistical Package for Social Science (IBM SPSS version 24) software. A descriptive analysis was performed as the mean ± SD, median, and interquartile range (IQR). The normality of variables was analyzed using the Shapiro–Wilk test. The differences among the groups were analyzed using the Chi-square test. The parametric parameters were analyzed with Student's *t*-test, and the nonparametric parameters were analyzed with the Mann–Whitney U-tests. A comparison between more than two groups was performed using the one-way analysis of variance (ANOVA) and Kruskal–Wallis test. Paired comparisons were performed with the Tamhane and Bonferroni tests. A multivariate logistic regression analysis was performed to determine the association with independent parameters for CA and calculated odds ratios (ORs) with a 95% confidence interval (CI). The predictive power of variables, cutoff values, sensitivity, and specificity was analyzed using a receiver operating characteristic (ROC) curve for CA patients. A $P < 0.05$ was considered statistically significant.

Results

Of 304 patients, 204 had AA (groups 1 and 2) and 100 control patients (group 3) were evaluated in this study. There were 138 (45.4%) patients in group 1,

Table 1: Comparison of laboratory and demographic parameters in groups

	NCA (Group 1) *n*=138	CA (Group 2) *n*=66	CG (Group 3) *n*=100	*P*	*P*1*	*P*2*	*P*3*
Gender							
Female	36 (26%)	8 (12%)	65 (65%)	<.001	0.03	<.001	<.001
Male	102 (74%)	58 (88%)	35 (35%)				
Age (years)							
Median (IQR)	28 (22)	45 (26)	48 (22)	<.001	<.001	<.001	NS
(Min-Max)	(14-76)	(17-68)	(16-80)				
WBC count							
(Mean) (×10^9/L)	12.46±4.15	15.01±4.22	7.64±1.69	<.001	<.001	<.001	<.001
(Min-Max)	(4.6-24.2)	(7.1-28.5)	(4.4-11.6)				
PDW							
(Mean) (fL)	16.09±0.79	16.50±0.93	15.89±0.89	0.01	0.01	NS	<.001
(Min-Max)	(11.8-18.0)	(15.1-20.1)	(11.2-17.3)				
MPV							
(Mean) (fL)	9.03±1.29	9.50±1.42	10.04±1.34	<.001	NS	<.001	0.05
(Min-Max)	(6.6-13.9)	(5.9-13.1)	(6.4-13.3)				
RDW							
(Mean) (%)	12.95±1.64	13.65±1.88	13.77±1.68	<.001	0.03	<.001	NS
(Min-Max)	(9.9-22.4)	(11.3-21.4)	(10.7-23.3)				
CK (U/L)							
Median (IQR)	102.5 (88)	85.5 (117)	62.0 (42)	<.001	NS	<.001	0.02
(Min-Max)	(23-1902)	(21-1135)	(17-136)				
Bilirubin (mg/dl)							
Median (IQR)	0.6 (0.5)	0.8 (0.7)	0.8 (0.3)	0.02	NS	NS	NS
(Min-Max)	(0.2-2.7)	(0.2-6.6)	(0.4-1.5)				

P: Three-group comparison with the one-way ANOVA or Kruskal-Wallis test; *P*1: Comparison between acute NCA and CA patients; *P*2: Comparison between NCA patients and the CG; *P*3: Comparison between CA patients and the CG; *: Two-group comparison with the Mann-Whitney U-test or Tamhane test (one-way ANOVA); WBC: White blood cell; PDW: Platelet distribution width; MPV: Mean platelet volume; RDW: Red cell distribution width; CK: Creatine kinase; IQR: Interquartile range; fL: Femtoliter; NS: Nonsignificant

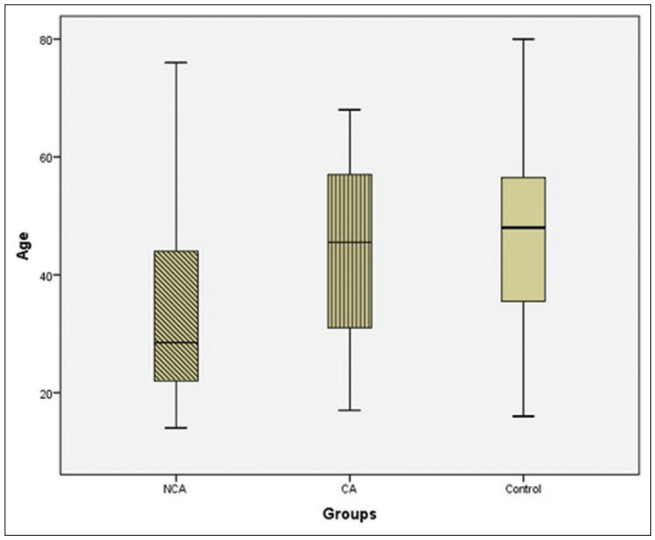

Figure 1: Age variation analyses between the groups

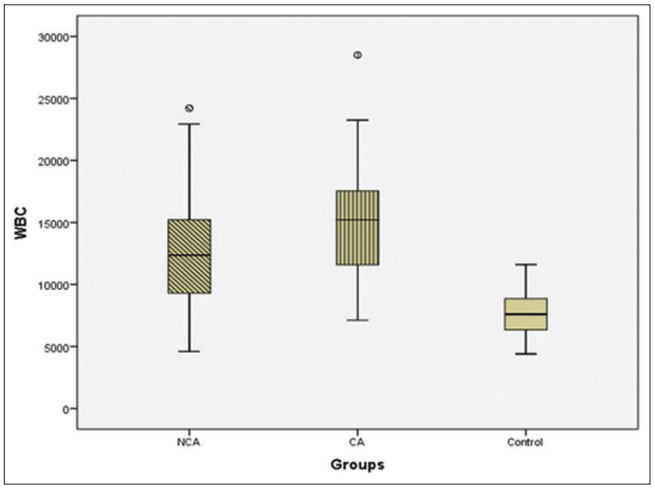

Figure 2: WBC variation analyses between the groups

66 patients (21.7%) in group 2, and 100 (32.9%) patients in group 3. Group 1 was comprised of 102 (74%) male and 36 (26%) female patients; group 2 was comprised of 58 (88%) male and 8 (12%) female patients; and group 3 was comprised of 35 (35%) male and 65 (65%) female patients. The median age (IQR) was 39 (28) years, ranging from 14 to 80 years.

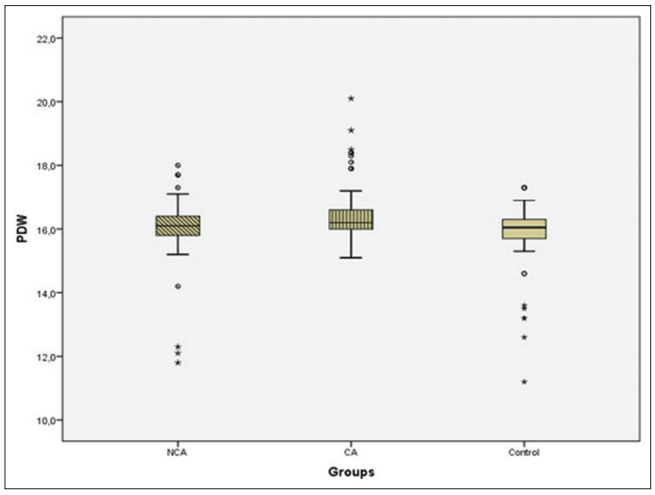

Figure 3: PDW variation analyses between the groups

Table 2: Independent risk factors for CA according to the multivariate regression analysis

	OR	95% confidence interval	*P*
Age	1.023	1.000-1.045	0.04
Gender (male)	3.718	1.501-9.213	0.005
WBC	1.000	1.000-1.000	0.002
PDW	2.129	1.301-3.484	0.003
MPV	1.129	0.883-1.445	NS
RDW	1.169	0.969-1.409	NS
CK	1.000	0.999-1.002	NS
Bilirubin	1.343	0.884-2.040	NS

WBC: White blood cell; PDW: Platelet distribution width; RDW: Red cell distribution width; MPV: Mean platelet volume CK: Creatine kinase; NS: Nonsignificant

Table 3: Predictive power of variables according to the ROC analysis, cutoff values, sensitivity, and specificity for CA

	Cutoff	AUC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	*P*
Age	>45.5	0.589	50.0%	65.1%	0.03
WBC count	>13.8×10^9/L	0.790	63.4%	81.1%	<.001
PDW	>16.95 fL	0.602	20.0%	95.4%	0.01

AUC: Area under the receiver operating characteristic curve; WBC: White blood cell; PDW: Platelet distribution width; MPV: Mean platelet volume; CI: Confidence interval

The median age was 28 (14–76) in group 1, 45 (17–68) in group 2, and 48 (16–80) in group 3 [Figure 1]. The mean WBC levels in groups 1, 2, and 3 were 12.46 ± 4.15, 15.01 ± 4.22, and 7.64 ± 1.69 × 10^3/mm^3, respectively. The WBC level was significantly higher in group 2 (P < .001; Figure 2). The mean PDW values in groups 1, 2, and 3 were 16.09 ± 0.79, 16.50 ± 0.93, and 15.89 ± 0.89 fL, respectively, and a statistically significant difference was found between all groups (P = 0.01; Figure 3). There was no difference between groups 1

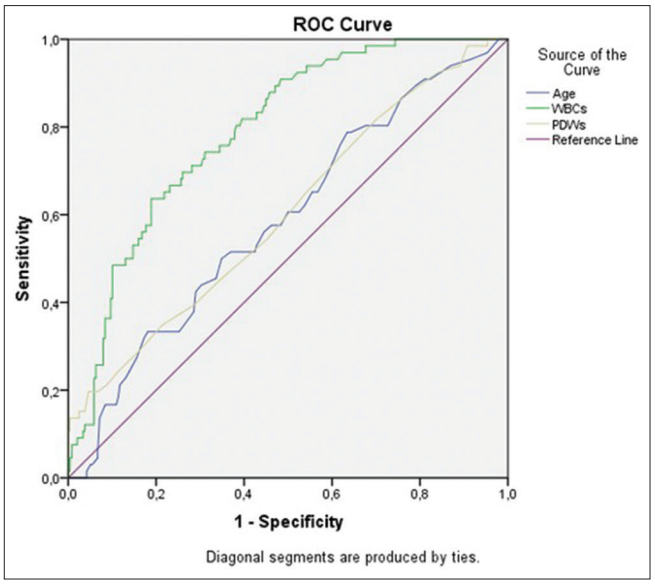

Figure 4: Receiver operating characteristic (ROC) curve analyses for the predictors of CA

and 3 (P > 0.05). The mean MPV values in groups 1, 2, and 3 were 9.03 ± 1.29, 9.50 ± 1.42, and 10.04 ± 1.34 fL, respectively. MPV levels were significantly different between the groups (P < .001). The mean RDW levels in groups 1, 2, and 3 were 12.95 ± 1.64, 13.65 ± 1.88, and 13.77 ± 1.68%, respectively, and there was a difference between all groups (P < 0.05).

The median CK values in groups 1, 2, and 3 were 102.5 (88) U/L, 85.5 (117) U/L, and 62.0 (42) U/L, respectively. CK levels were significantly different in the groups (P = 0.01). There was no statistical significance in groups 1 and 2, although the CK level was lower in group 1 (P > 0.05). The median bilirubin values in groups 1, 2, and 3 were 0.6 (0.5) mg/dl, 0.8 (0.7) mg/dl, and 0.8 (0.3) mg/dl, respectively [Table 1].

The multivariate regression analysis was used to define the association with independent parameters for CA. The analysis demonstrated that age (OR: 1.023; 95% CI: 1.000–1.045; P = 0.04), male sex (OR: 3.718; 95% CI: 1.501–9.213; P = 0.005), WBC count (OR: 1.000; 95% CI: 1.000–1.000; P = 0.002), and PDW count (OR: 2.129; 95% CI: 1.301–3.484; P = 0.003) were independently associated with complicated appendicitis (CA). However, RDW (OR: 1.169; 95% CI: 0.969–1.409; P = 0.10), MPV (OR: 1.129; 95% CI: 0.883–1.445; P = 0.33), CK (OR: 1.000; 95% CI: 0.999–1.002; P = 0.54), and bilirubin levels (OR: 1.343; 95% CI: 0.884–2.040; P = 0.16) were not associated with CA according to the multivariate regression analysis [Table 2].

In the ROC analysis, age, WBC, and PDW levels were established as predictive in the differential

diagnosis of CA [Figure 4]. The cutoff value for age was established as 45.5, with a sensitivity of 50.0% and a specificity of 65.1% (AUC: 0.589; 95% CI: 0.512–0.665; P = 0.03). The cutoff value for WBC was established as 13.8 × 10^9/L, with a sensitivity of 63.4% and a specificity of 81.1% (AUC: 0.790; 95% CI: 0.735–0.846; P = 0.000). The cutoff value for PDW was established as 16.95 fL, with a sensitivity of 20.0% and a specificity of 95.4% (AUC: 0.602; 95% CI: 0.524–0.681; P = 0.01) [Table 3].

Discussion

An inaccurate diagnosis and late surgical intervention in CA have significant importance in terms of the severity of the disease. Therefore, the differential diagnosis of NCA and CA is important in unusual cases.[13] Some laboratory tests may contribute to the diagnosis of AA but are not successful in distinguishing CA and NCA themselves. For this purpose, the inexpensive and appropriate inflammatory markers that can be detected by routine blood tests have been examined to evaluate their value in diagnosing AA and CA in many studies.[14,15] Despite all technological advances in recent years, the improvement in the sensitivity and accuracy of diagnostic tests for NCA and CA patients is not yet remarkable.[16]

We found significant differences between the groups in terms of age and sex. The mean age was found to be higher in CA patients than in NCA patients. This issue may be clarified by the difficulties in diagnosing CA in elderly patients and by their possible immune system weakness compared with younger patients.

WBC count is the most studied laboratory parameter and initial sign in patients with AA, and the elevation of WBC level in NCA is a fact. Dinc T *et al*.[17] demonstrated higher WBC values in patients with CA than in the CG. We found that the WBC count was higher in patients with NCA than in the CG. We also showed that the WBC count was statistically higher in patients with CA than in patients with NCA and the CG. Dinc B *et al*.[18] and Narci *et al*.[19] noted that the sensitivity, specificity, and cutoff point for WBCs were 73%–94%, 10.6 × 10^9/L, 53%–100%, and 10.4 × 10^9/L, respectively. Similar to the literature, we determined a sensitivity of 63.4%, a specificity of 81.1%, and a cutoff point of 13.8 × 10^9/L for WBCs.

PDW is a value that shows the heterogeneity of thrombocyte volume. The assessment of PDW and MPV ensures a preferable clarification as regards thrombocyte volume disturbance and increased growth of megakaryocytes.[20] MPV and PDW levels suggest platelet immaturity and young platelets that are delivered into the peripheral blood circulation.[11] Fan *et al*.[15] noted that PDW levels increased in patients with CA, and a diagnostic algorithm for CA may include the WBC count and PDW. Aydogan *et al*.[11] showed that both MPV and PDW were important signals in the early detection of the perforation risk in AA. Dinc B *et al*.[18] demonstrated higher WBC and PDW levels in patients with CA than in the CG. We showed higher MPV and PDW values in patients with CA than in patients with NCA. The elevation in MPV value was not statistically significant, but we believed that a high PDW level is a usable laboratory test in determining CA patients. The high specificity of PDW may imply an early diagnosis of CA in our study. However, our data on medically treated and nonoperated patients were not included in this study. Therefore, the low sensitivity of PDW can be attributed to the inclusion of only operated patients in our study.

The MPV level shows both inflammation and thrombosis as a sign of platelet activation. Increased levels of MPV occur in the case of chronic disease.[21] Danese *et al*.[22] postulated that the decreased MPV level may utilize activated platelets in the intestinal vasculature. Albayrak *et al*.[10] showed decreased MPV levels in patients with AA compared with the CG. Similarly, the MPV level was found to be significantly lower in patients with CA and NCA than in the CG in our study (P < .001). However, there was no difference between CA and NCA patients in terms of MPV level, and the decrease in MPV levels was not found to be associated with CA according to the multivariate logistic regression analysis.

Elevated RDW levels were associated with elevated inflammatory markers, such as sedimentation rate, CRP, and interleukin-6 level.[23-25] These mediators can induce larger reticulocytes to enter the peripheral circulation. Thus, increased RDW levels occur in chronic inflammation compared with acute stages.[23] Narci *et al*.[19] found a significantly lower RDW level in AA patients than in the CG. Similarly, the mean RDW level was higher in CA patients than in NCA patients in our study, but it was not associated with CA according to the multivariate logistic regression analysis.

Ischemic or hemorrhagic intestinal infarcts stimulate bacterial growth and give rise to mucosal damage. The breakdown of intestinal smooth muscle cells causes the release of CK isoenzymes. Thus, serum CK activity is increased in intestinal ischemia.[12] Graeber *et al*.[26] showed that serum CK isozyme levels were significantly elevated following infarction in dogs. The damage to the appendix wall causes the translocation of bacteria and endotoxins released from the appendiceal lumen into the portal system in AA. These cytokines may give rise to

intrahepatic cholestasis and elevated bilirubin levels.[27] McGowan *et al*.[9] suggested that bilirubin and CRP are the markers of perforation in appendicitis but are not accurate enough to be diagnostic. We did not find a difference between CA and NCA patients in terms of CK and bilirubin levels in our study. Additionally, our studies did not demonstrate the predictive value of CK and bilirubin elevation in CA patients.

Conclusion

Age, WBC count, and PDW level were determined predictively in the differential diagnosis of CA patients in our study. The elevation of WBC level in NCA is a well-known fact in most studies. Although there is an increase in the WBC level in NCA, elevated PDW and higher WBC level may help us anticipate the severity of CA, especially in elderly patients. We believed that the increase in PDW and higher WBC level were valuable in differentiating the diagnosis of CA from NCA and that this may be a feasible approach when deciding on surgery.

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Conflicts of interest

There are no conflicts of interest.

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